

ORIGINAL ARTICLE

SPACE-TIME PATTERN OF AIDS MORTALITY*
PADRÃO ESPAÇO-TEMPORAL DA MORTALIDADE POR AIDS
PATRÓN ESPACIO-TIEMPO DE MORTALIDAD DEL SIDA*

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ABSTRACT







Objective: to analyze the spatial-temporal distribution of AIDS mortality. **Method:** this is a quantitative, descriptive study, which evaluated 959 aids deaths reported through the Mortality Information System. The temporal trend was analyzed using the Joinpoint Regression Program, version 4.6.0.0, and the Scan scanning was used to evaluate the formation of purely spatial clusters of deaths, considering a significance level of 5%. **Results:** most deaths occurred among males (71.1%), with seven years of schooling or less (79.6%), of *pardo* race (72.2%) and age group from 30 to 39 years (69.2%). There was a statistically significant increase in AIDS mortality of 5.2% per year ($p < 0.001$; 95% CI: 1.0-9.5). The spatial scanning pointed to a statistically significant cluster of deaths ($p < 0.0001$), which covered 18 municipalities, including Oeiras, Parnaíba and those in the metropolitan region of Teresina. **Conclusion:** the analysis of temporal and spatial trends showed a significant increased mortality over the period studied, as well as the presence of a cluster of deaths that covered 18 municipalities, including Teresina, Oeiras and Parnaíba. **Descriptors:** HIV; Acquired Immunodeficiency Syndrome; Spatial Analysis; Geographic Mapping; Mortality; Epidemiology.

RESUMO

Objetivo: analisar a distribuição espaço-temporal da mortalidade por aids. **Método:** trata-se de um estudo quantitativo, descritivo, que avaliou 959 óbitos por Aids notificados por meio do Sistema de Informação sobre Mortalidade. Analisou-se a tendência temporal por meio do *software Joinpoint Regression Program*, versão 4.6.0.0, e a varredura *Scan* foi empregada para avaliar a formação de *clusters* puramente espaciais de óbitos, considerando-se um nível de significância de 5%. **Resultados:** verifica-se que a maioria das mortes ocorreu entre indivíduos do sexo masculino (71,1%), com sete anos de estudo ou menos (79,6%), de raça parda (72,2%) e faixa etária de 30 a 39 anos (69,2%). Registrou-se um aumento estatisticamente significativo da mortalidade por Aids de 5,2% ao ano ($p < 0,001$; IC95%: 1,0-9,5). Observa-se que a varredura espacial apontou para um *cluster* de óbitos estatisticamente significativo ($p < 0,0001$), que abrangeu 18 municípios, incluindo Oeiras, Parnaíba e os da região metropolitana de Teresina. **Conclusão:** nota-se que a análise das tendências temporal e espacial demonstrou um aumento significativo da mortalidade ao longo do período estudado, bem como a presença de um aglomerado de óbitos que abrangeu 18 municípios, incluindo Teresina, Oeiras e Parnaíba. **Descritores:** HIV; Síndrome da Imunodeficiência Adquirida; Análise Espacial; Mapeamento Geográfico; Mortalidade; Epidemiologia.

RESUMEN

Objetivo: analizar la distribución espacio-temporal de la mortalidad por SIDA. **Método:** se trata de un estudio cuantitativo y descriptivo que evaluó 959 muertes por SIDA reportadas a través del Sistema de Información sobre Mortalidad. La tendencia temporal se analizó utilizando el *software Joinpoint Regression Program*, versión 4.6.0.0, y el escaneo *Scan* se utilizó para evaluar la formación de grupos puramente espaciales de muertes, considerando un nivel de significancia del 5%. **Resultados:** se verificó que la mayoría de las muertes ocurrieron entre los varones (71,1%), con siete años de escolaridad o menos (79,6%), de raza parda (72,2%) y grupos de edad de 30 a 39 años (69,2%). Hubo un aumento estadísticamente significativo de la mortalidad por SIDA del 5,2% anual ($p < 0.001$; IC del 95%: 1,0-9,5). Se observó que el escaneo espacial apuntaba a un grupo estadísticamente significativo de muertes ($p < 0.0001$), que abarcaba 18 municipios, incluyendo Oeiras, Parnaíba y los de la región metropolitana de Teresina. **Conclusión:** se observa que el análisis de las tendencias temporales y espaciales mostró un aumento significativo de la mortalidad durante el período estudiado, así como la presencia de un grupo de muertes que abarcó 18 municipios, entre ellos Teresina, Oeiras y Parnaíba. **Descriptor:** VIH; Síndrome de Inmunodeficiencia Adquirida; Análisis Espacial; Mapeo Geográfico; Mortalidad; Epidemiología.

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*Article extracted from the Doctoral Thesis << Space-Time distribution of cases and deaths from AIDS in Piauí and its relationship with Health Social Determinants >>. State University of Ceará/UECE, 2018.

How to cite this article

Maranhão TA, Alencar CH, Ribeiro LM, Sousa GJB, Abreu WC, Pereira MLD. Space-time pattern of aids mortality. J Nurs UFPE on line. 2020;14:e244407 DOI: <https://doi.org/10.5205/1981-8963.2020.244407>

INTRODUCTION

The report of the United Nations Joint Program on HIV/AIDS (UNAIDS) revealed that the global increase in coverage of Antiretroviral Therapy (ART) increased the survival and quality of life of people living with HIV/AIDS (PLWHA), characterizing it as a chronic disease. The availability of ART was the main contributor to the reduction in 48.0% of AIDS-related deaths, from 1.9 million to 1 million deaths in 2005 and 2016, respectively.¹

Among the emerging countries in providing free treatment for HIV-infected people, Brazil was one of the pioneers in 1996. This policy of universal access and free periodic follow-up offered by the Unified Health System (UHS) resulted in a sharp drop in mortality rates associated with the disease.² It is noteworthy that, currently, Brazil has one of the highest coverage of ART among low- and middle-income countries.³

After the implementation of the treatment policy for all, which determines the immediate introduction of ART to all HIV-positive people, regardless of their immunological status, the standardized AIDS mortality rate in Brazil decreased 7.2%. However, this decrease is not observed in all Brazilian regions, because only the South, Southeast and Midwest regions showed decreases in the number of deaths, whereas, in the North and Northeast regions, the trend is an increase in the number of deaths.⁴

Despite the efforts, in the period from 2000 to 2014, the HIV/AIDS mortality increased over 50% in 44.4% of the Brazilian states. In the state of Piauí, the increase in deaths in this period was 140.0%, since, in 2000, the mortality rate was 1.5 deaths/100,000 inhabitants and, in 2014, the death rate jumped to 3.6 deaths/100,000 inhabitants.⁵

Therefore, since populations have distinct social compositions that evidence disparities and that mortality patterns do not occur randomly in space, but in ordered patterns that express underlying causes, a spatial analysis represented by means of maps in geographic location and distribution of health events in the territory is essential.⁶ This type of space analysis is performed through geoprocessing tools for health events, which have been growing in Brazil in recent years and being applied in investigations that portray the spatial distribution of AIDS in the most diverse populations.⁷⁻¹⁰

OBJECTIVE

- To analyze the spatial and temporal distribution of AIDS mortality.

METHOD

This is a quantitative, descriptive study, whose geographical area of interest is the state of Piauí,

located in Northeastern Brazil, with a total area of 251,529.186 km², which corresponds to 16.2% and 2.9% of the total areas of the Northeast and Brazil, respectively. Among the nine states of the Northeast region, it is the third largest in terms of territorial surface area, being surpassed only by Bahia and Maranhão. Currently, Piauí includes 224 cities divided into four development mesoregions: Northern Piauí; Midnorthern Piauí; Southeastern Piauí and Southwestern Piauí.¹¹

The data of this investigation are of the secondary type and were extracted from the Mortality Information System (SIM), whose information, in turn, comes from death certificates. The information collected refer to the patients who died from 2007 to 2015, whose underlying cause of death certificates was AIDS. Therefore, only those whose codes B20 to B24 were cited according to the 10th International Classification of Diseases (ICD-10) were selected. The databases were made available by the Coordination of Communicable Diseases of the State Health Bureau of Piauí (SES-PI) as Tabnet file.

The variables analyzed were: year of death; sex; age group; race/color; years of schooling and marital status. Information regarding the city of residence of the patients was also collected to allow mapping according to the city of origin, as well as to classify them as residents in the capital or in the inland.

TabWin software, v.4.14[®], was used to calculate mortality rates. The numerator of the formula was the number of deaths in each year and, the denominator, the population of each city of Piauí, according to the 2010 Demographic Census and population estimates of the other intercensus years (2007 to 2009 and 2011 to 2015), multiplying the value per 100,000 inhabitants.¹²

In the exploratory analysis of the epidemiological profile of AIDS deaths, the categorical quantitative variables were described in absolute and relative frequencies and presented through tables. In addition to the univariate descriptive analysis, bivariate analyses were performed using Pearson's chi-square test (χ^2) to test associations between schooling by years of study and sex, year of death and place of residence. For this, the software R, version 3.3.3[®], was used, considering a $p < 0.05$ as necessary for the rejection of the null hypothesis.

The free software Joinpoint Regression Program, version 4.6.0.0, was used to analyze the temporal trend of mortality. This program performs segmented linear analysis, with the logarithmic transformation of the values. It was tested whether one or more points should be added to the linear model by Monte Carlo permutation, i.e., it was evaluated whether a line with multiple segments describes the model better than just a line.¹³

The annual percentage change (APC) was calculated using a 95% confidence interval (95% CI), in which a negative APC value indicates a decreasing trend and a positive value points to an increasing trend. Each inflection point added to the model represents a change in the linear trend. Thus, the model was adjusted, assuming that the number of inflection points could range from zero (only one segment) to two (three segments) over the years. A significance level of 5% was established to test the null hypothesis that the APC of the series was equal to zero. Thus, for the analysis of APC, the results with $p<0.05$ or 95% CI only positive (increasing trend) or only negative (decreasing trend) were considered significant.¹³

The formation of purely spatial clusters of AIDS deaths was analyzed using the spatial statistical technique of Scan scanning, using the Software SatScan, v.9.6®. This method consists of a circular geographic window that moves through the area of interest and, in this scanning, the circle includes different sets of neighboring areas, which are considered candidates to represent a possible cluster of the event.

In this study, clusters of high AIDS mortality rates were identified, using a circular base window that corresponded to 50% of the population at risk, with a significance level of 5%. The probabilistic model considered in the application of Scan spatial statistics was the Poisson model, which considers that the number of events in each area is distributed according to the

population at risk, that is, the occurrence is proportional to the size of the population.⁶

The Scan method also allowed building spatial maps of Relative Risk (RR) for the formation of clusters in the analyzed period (2007-2015). This indicator represents the intensity of the occurrence of AIDS deaths in an area in relation to all regions analyzed in the study. When $RR < 1$, the relative risk of a given area is below the risk of the region as a whole. Contrarily, when $RR > 1$, the relative risk of a specific area is greater than the risk of the entire region analyzed and, when the values of both are equal to one, the risk is equal for both.

All ethical and legal aspects recommended by Resolution 466/12 were respected. After authorization by SES-PI, the information was collected confidentially, omitting the identification of individuals. This study was submitted and approved by the Research Ethics Committee of the State University of Piauí under opinion n. 1.665.775 and CAAE n. 58034216.3.1001.5209.

RESULTS

Table 1 shows that there were 959 deaths from AIDS in the state of Piauí in the period of study.

Table 1. Sociodemographic characterization of deaths from AIDS, Piauí, Brazil, 2007-2015. Parnaíba (PI), Brazil, 2018. (N=959)

Characteristics	n	%
Sex		
Male	682	71.1
Female	277	28.9
Race*		
Pardo	633	72.2
Black	115	14.6
White	115	13.1
Indigenous	1	0.1
Age group**		
< 9 years	14	1.5
10 - 19 years	12	1.2
20 - 29 years	164	17.1
30 - 39 years	321	33.5
40 - 49 years	265	27.7
50 - 59 years	113	11.9
60 years or more	68	7.1
Years of study***		
None	71	9.2
1 - 3 years	216	28.1
4 - 7 years	256	33.3
8 - 11 years	173	22.5
12 years or more	53	6.9
Marital status****		
Married or in a consensual union	236	28.4
Unmarried	594	71.6

*82 deaths were excluded, which included the race as “ignored”. **Two deaths that included age as “ignored” were excluded. ***190 cases were excluded, which included the level of education as “ignored”. ****129 deaths were excluded, with marital status as “ignored”.

Table 2 shows the distribution of AIDS deaths according to schooling by years of study, year of death, gender and place of residence. It is pointed out that no relationship of dependence was observed between schooling and the year of death ($p=0.0983$) and between schooling and sex

($p=0.3849$). However, there was a statistically significant association ($p<0.001$) between schooling and place of residence, considering that people who died from AIDS living in the capital, Teresina, had more years of schooling compared to individuals living in the inland of the state.

Table 2. Characterization of AIDS deaths according to schooling by years of study and year of death, sex and place of residence. Piauí, Brazil, 2007-2015. Parnaíba (PI), Brazil, 2018. (N=959)

Variables	Schooling by years of study*										$\chi^2\chi^2^*$ p-value	
	None		1 - 3		4 - 7		8 - 11		≥12			Total
	n	%	N	%	n	%	n	%	n	%	N	
Year of death*												
2007	4	6.1	23	34.8	25	37.9	12	18.2	2	3.0	66	0.0983
2008	2	3.2	13	20.7	29	46.0	13	20.6	6	9.5	63	
2009	8	9.9	23	28.4	28	34.6	18	22.2	4	4.9	81	
2010	8	10.4	17	22.1	27	35.0	21	27.3	4	5.2	77	
2011	4	5.6	24	33.3	26	36.1	17	23.6	1	1.4	72	
2012	9	7.6	26	21.8	40	33.6	31	26.1	13	10.9	119	
2013	11	11.0	34	34.0	27	27.0	24	24.0	4	4.0	100	
2014	14	13.9	26	25.7	33	32.7	21	20.8	7	6.9	101	
2015	11	12.2	30	33.3	21	23.3	16	17.8	12	13.4	90	
Sex												
Male	49	69.0	152	70.4	178	69.5	133	76.9	41	77.4	553	0.3849
Female	22	31.0	64	29.6	78	30.5	40	23.1	12	22.6	216	
Place of residence												
Capital	18	25.4	94	43.5	145	56.6	108	62.4	37	69.8	402	<0.0001
Inland	53	74.6	122	56.5	111	43.4	65	37.6	166	30.2	367	

*190 deaths were excluded in which schooling was “ignored”.

Figure 1 shows the evolution of the AIDS mortality rate in Piauí from 2007 to 2015 for the general population and for both sexes. The highest rates are related to males. In addition, mortality

showed a trend of growth over time, and in 2012, the highest coefficients were recorded (6.2, 4.3 and 2.48 deaths per 100,000 inhabitants for males, general population and females, respectively).

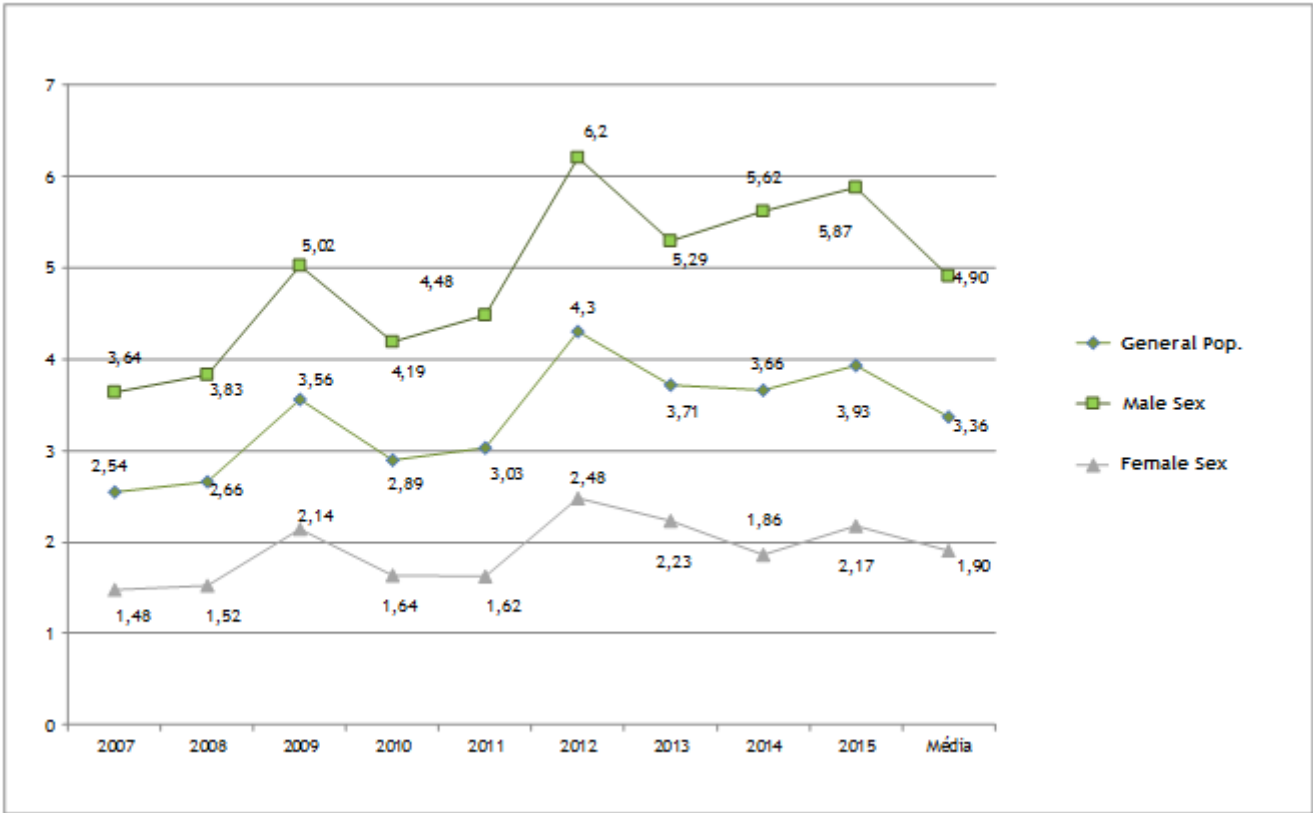


Figure 1. AIDS mortality coefficient in the general population and in the male and female sexes. Piauí, Brazil, 2007-2015. Parnaíba (PI), Brazil, 2018.

The Joinpoint analysis confirms the constant linear trend observed in the evolution of mortality rates, since there was no need to add inflection points that characterize trend changes. In this sense, there was a statistically significant increase in the mortality rate from AIDS by 5.2% per year ($p<0.001$; 95% CI: 1.0-9.5) (Figure 2).

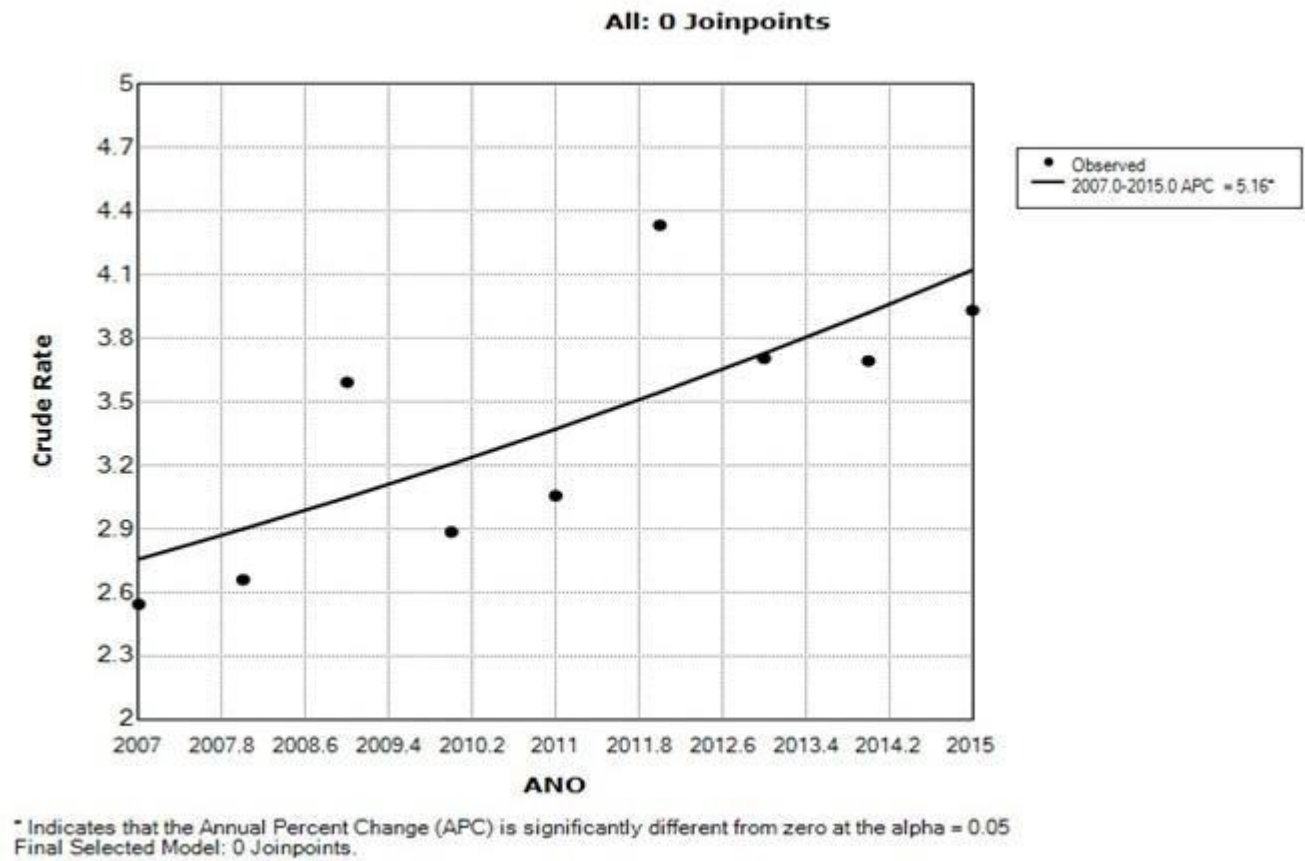


Figure 2. Joinpoint time trend of AIDS mortality. Piauí, Brazil, 2007-2015. Parnaíba (PI), Brazil, 2018.

Figure 3B shows that cities in lighter green have a relative risk for AIDS mortality lower than that of the state as a whole. The cities of Guadeloupe (RR = 3.75) and Caridade do Piauí (RR = 4.12), in darker green, present the highest relative risks of the state.

Figure 3C shows that the analysis of purely spatial scanning by the Scan method identified three clusters at high risk for AIDS deaths. It is noteworthy that the primary cluster and the only statistically significant cluster ($p<0.0001$), with a radius of 47.36 km and RR of 1.86, covered 18 cities, including those in the metropolitan region of Teresina, in addition to Oeiras, in the Southeast mesoregion, and Parnaíba, located in Northern Piauí.

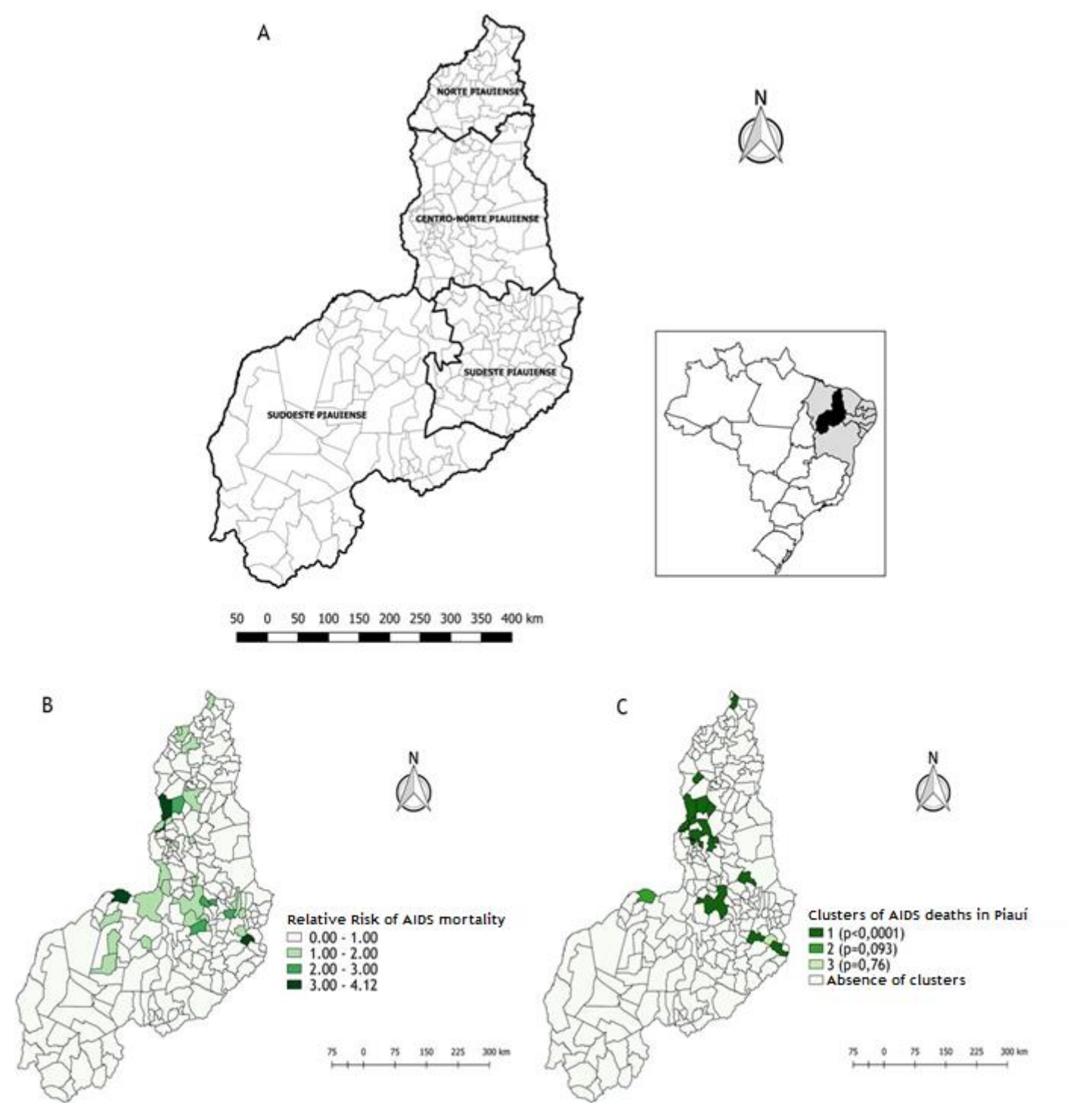


Figure 3. State of Piauí according to its development mesoregions (A), Relative risk of deaths from AIDS (B) and Clusters of deaths from AIDS (C). Piauí, Brazil, 2007-2015. Parnaíba (PI), Brazil, 2018.

Table 3 presents detailed information of the clusters of AIDS deaths identified through purely spatial Scan scanning analysis.

Table 3. Characterization of spatial clusters of AIDS-related deaths defined by purely spatial scanning statistics. Piauí, Brazil, 2007-2015. Parnaíba (PI), Brazil, 2018.

Cluster	N. of cities	Radius (km)	N. of cases	Expected n. of cases	RR*	LLR**	p-value
1	18	47.36	636	340.83	1.86	187.77	<0.0001
2	1	0.00	12	3.22	3.72	7.03	0.093
3	1	0.00	6	1.46	4.09	3.93	0.76

* RR: Relative risk for the cluster compared to the rest of the State. ** LLR: Logarithmic Likelihood Ratio Test.

DISCUSSION

This study unveiled a linear trend of increased AIDS mortality rate in Piauí over the studied period. Data from the Ministry of Health indicate that deaths from AIDS-related causes have

important regional differences, with trend to increase in the North and Northeast regions of the country.¹⁴ A study on HIV/AIDS mortality in Brazil stated that better mortality indicators would be expected, since Brazil has a well-established

PLWHA care system, with free and universal access to ART.⁵

Several factors that lead to increased death rates are listed, one of which is low HIV testing both in the general population and among those belonging to key populations, especially men who have sex with men.¹⁵ Moreover, many individuals are still diagnosed when they are already in more advanced stages of the syndrome, thus making essential the diagnosis at the beginning of HIV infection.¹⁶ Other contributing factors for high rates of AIDS deaths encompass low adherence and non-adherence to antiretroviral treatment among individuals followed up in reference services. This problem is an important threat to the successful treatment, as it is directly associated with therapeutic failure while facilitating greater resistance of HIV to available medications.¹⁷⁻⁸

In Piauí, the number of men who die from AIDS-related causes is more than twice the number of women. An investigation showed the greatest vulnerability to AIDS illness and deaths in the male population, especially among young people. Historically, men is known to seek medical care less than women do, due to social, cultural and gender patterns that do not associate health care with male behavior.^{8,19} A UNAIDS report revealed that men are less likely to take HIV testing and seek antiretroviral treatment compared to women. In addition, less than half of HIV-positive men are treated worldwide, as opposed to 60.0% of women.²⁰ The non-search for health care is believed to lead to postponement of the diagnosis of seropositivity and the late onset of ART, which often only occur in the presence of advanced disease.²¹

Most AIDS cases and deaths in Piauí occurred in patients of the *pardo* color. The second most prevalent race was black. The high rate of AIDS mortality among *pardos* and black individuals may be associated with the historical social exclusion of this population. Therefore, being part of a group of people of a certain race says a lot about their living conditions, as well as about the (non-)access to health services. The majority of the black population is characterized as being more concentrated in regions with scarcity of resources and precarious sanitation, housing, education and work conditions, which intensifies their vulnerability to various diseases.²²

People who die from AIDS-related diseases were mostly in the age group of 30 to 49 years. This profile follows the national patterns of AIDS mortality according to age.⁴ The fact that most deaths include adult individuals at the peak of their productive phase is particularly worrisome, as it reveals the low life expectancy of the infected. When the diagnosis is made in due time and the HIV-positive individual has access and adheres satisfactorily to ART, his/her life

expectancy is expected to be almost equal to that of an HIV-negative individual.²³

A significant proportion of deaths of PLWHA in Piauí had low schooling, since these patients had not even completed Elementary School II (fifth to eighth grades). Researches recorded that the level of education of PLWHA is an important predictor of adherence to antiretroviral therapy^{18,24} and of early virological response among those who initiate ART.²¹

Although a higher percentage of deaths was observed in the capital, a significant proportion of residents in the inland of the state were observed. The large number of AIDS deaths in cities in the inland of Piauí is probably related to the precarious socioeconomic and structural characteristics that promote significant inequalities between these localities and the capital, where, in turn, there is greater infrastructure and circulation of wealth.²⁵ Therefore, the literature established an intimate relationship between mortality and social and economic status, because the longevity of people goes in the same direction as their living conditions.²⁶

There was statistical significance between the schooling of AIDS deaths and the place of residence, as patients living in the inland of the state had fewer years of schooling than the residents of the capital did. The capital is among the five largest cities in the state in population terms and, consequently, has greater structure and availability of educational resources and access to public and private schools, universities and technical and professional courses.²⁵

The spatial analysis demonstrated that the greatest relative risks for deaths are in two small cities: Guadalupe (Southwest mesoregion) and Caridade do Piauí (Southeast mesoregion). These cities have, in common, a low Municipal Human Development Index in the Education dimension (Caridade do Piauí - 0.426; Guadalupe - 0.542).²⁷ This datum is considered relevant, adding that an integrative literature review on the social determination of HIV/AIDS identified, in several studies, that the low educational level is associated not only with HIV infection, but also with deaths from AIDS.²⁸

There was also a statistically significant cluster of AIDS deaths that encompasses 18 cities, including Teresina, Parnaíba (Northern Piauí) and Oeiras (Southeast mesoregion), which are among the most populous cities in the state. This result corroborates the pattern of distribution of the disease in Brazil, where the highest concentration of the epidemic occurs mainly in large urban centers and metropolitan regions due to the intense flow of people who continuously interrelate.^{7,29}

Brazil has public policies and programs for the specialized monitoring of PLWHA installed in the

capitals and in large cities in the inland of the states. Health and social care networks of greater complexity are concentrated in Piauí, predominantly in the capital, Teresina.³⁰ Therefore, the most significant cluster of deaths in this territory is due to the immigration of individuals from the inland or other states seeking follow-up of more complex services when the disease is already installed (later evolving to death). In turn, the high rates of AIDS deaths located in Parnaíba, on the Piauí coast, may be related to the large influx of tourists who are attracted not only by the beautiful landscapes, but also by sex tourism.³¹

This study has some limitations that, however, do not make it impossible. The main one related to the use of secondary data, which may present inconsistencies regarding the quantity and quality of information. Furthermore, the mortality data obtained from the SIM may present incorrect classification of the underlying cause and underreporting of deaths from AIDS-related causes.

CONCLUSION

Most individuals who died from AIDS-related causes were male, *pardo* race, followed by black, unmarried, age group from 30 to 49 years and with schooling equal to or less than seven years of study. Moreover, a significant proportion of deaths occurred in the state capital, Teresina, where, in turn, concentrated most of those cases that had higher education, probably due to the greater presence of schools and universities in the capital compared to inland cities.

The temporal trend of AIDS mortality in the state pointed to a significant increase in rates over the period studied. The analysis of spatial distribution by the Scan scanning method showed the presence of a statistically significant spatial cluster of deaths, which covered 18 cities, including those in the metropolitan region of Teresina, in addition to Oeiras, in the Southeast mesoregion, and Parnaíba, located in Northern Piauí, near the coast. It is noteworthy that the cities of Guadalupe and Caridade do Piauí presented the highest relative risks for AIDS mortality in the state.

The results of this study are expected to contribute to understanding the epidemiology of mortality from AIDS-related causes in Piauí. Thus, the knowledge of the spatial and temporal distribution of deaths in this territory is believed to be of fundamental importance to analyze risks, prevent HIV infection, as well as to support specific interventions, especially those that stimulate adherence to antiretroviral therapy among PLWHA.

CONTRIBUTIONS

It is informed that all authors contributed equally in the design of the research project, collection, analysis and discussion of data, as well as in the writing and critical review of the content with intellectual contribution and the approval of the final version of the study.

CONFLICT OF INTERESTS

Nothing to declare.

FUNDING

Coordination for Higher Level Personnel Improvement (CAPES).

Foundation for Research Support of the State of Piauí (FAPEPI).

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Submission: 2020/03/02

Accepted: 2020/05/15

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